REMARKS

In an Office Action mailed April 18, 2001 pending claims 18 through 32 were variously rejected under 35 U.S.C. §112, first and second paragraphs, and §103(a). In view of the following amendments and remarks, reconsideration is respectfully requested.

I. The Subject Matter of the Claims

In general, the subject matter of the claims relates to methods for detecting ICAM-4 in a sample.

II. Support for the Claims

New claims 33 through 41 are fully supported by the specification. For example in claim 33, reference to a human neuronal ICAM-4 polypeptide as set out in SEQ. ID NO. 28 can be found at page 37, lines 6-7.

ICAM-4 specific monoclonal antibodies 179I and 179H and the hybridomas producing these monoclonal antibodies are set forth in Example 14, page 43 line 15 through page 44 line 16.

Monoclonal antibody 173E, specific for domains 1-3 of the human ICAM-4 polypeptide, and antibodies 179I and 179H, specific for domains 4-8 of the ICAM -4 polypeptide, are useful in detection assays (as outlined in Examples 15, 16, and 18) for the measurement of ICAM-4 levels in either a sample containing full length recombinant peptide or samples derived from serum or cerebrospinal fluid. The ICAM-4 detectable in samples derived from body fluids originates after neuronal trauma and subsequent release of ICAM-4 from the cell membranes into the cytoplasm, indicating that the ICAM-4 in samples is likely a soluble, truncated form of the full length ICAM-4 polypeptide. Detection of either the full length or a soluble truncated version of ICAM-4 by the monoclonal antibodies of the invention, which show specificity for different domains of the polypeptide, demonstrates that the full length human ICAM-4 polypeptide is not required for detection by the specific anti-ICAM-4 monoclonal antibodies, but that a fragment of the polypeptide can be detected by these monoclonal antibodies as well as the full length protein. Therefore, the disclosure supports the detection of an antigen

comprising an epitope specifically recognized by an anti-human neuronal ICAM-4 antibody as set forth in claim 33.

Claims 33 through 41 include no new matter.

III. The Outstanding Rejections

A. The Rejections of Claims Under 35 U.S.C. §112, First Paragraph, May Properly Be Withdrawn

The Rejection of Claims 18, 23, and 28

The Examiner rejected amended claims 18, 23, and 28 under 35 U.S.C. §112, first paragraph, for allegedly lacking written descriptive support in the specification. Specifically, the Examiner asserted that the claims embrace a genus of specific binding partners for ICAM-4. The Applicant submits that the insertion of new claims 33 through 41 which recite antibodies and their use obviates this rejection and renders the Examiner's argument moot.

B. The Rejection of Claims Under 35 U.S.C. §103(a), Second Paragraph, May Properly Be Withdrawn

Claims 18, 19, 21-24, 26, 27, and 30-32 were rejected under 35 U.S.C. §103(a) as being directed to subject matter assertedly rendered obvious by the disclosure of Oka et al., Neurosci. 35:93-103 (1990) [hereinafter "Oka"] in view of the disclosure of Yoshihara et al., Neuron 12:543 (1994) [hereinafter "Yoshihara"]. Claims 20 and 29 were also rejected under 35 U.S.C. §103(a) for being directed to subject matter allegedly rendered obvious by the disclosure of Oka in view of Yoshihara and further in view of Goding, Monoclonal Antibodies: Principals and Practice, Academic Press Inc, 1983, pp. 57-97 [hereinafter "Goding"]. The Applicant respectfully disagrees.

The Examiner asserts that the worker of ordinary skill in the art would have knowledge of the existence of both the rat and human homologs to ICAM-1, ICAM-2, and ICAM-3 and therefore be able to predict the existence of the human homolog to ICAM-4. The Examiner admits that the cited references above do not disclose assays using human ICAM-4 specifically. To the extent that the worker of ordinary skill may have speculated the existence of the human protein, this same worker certainly could not have speculated that the human protein would have the recited polypeptide sequence in

the specification. Accordingly, the worker of skill in the art would have *no* expectation of success in making and/or using the methods as claimed.

Likewise, with respect to Oka in light of Yoshihara in view of Goding, while the method of producing monoclonal antibodies is common knowledge to those skilled in the art, a worker skilled in the art could not have predicted the existence of anti-human ICAM-4 monoclonal antibodies as disclosed and claimed herein without the present disclosure, Without the disclosure of SEQ. ID NO. 28 the worker of ordinary skill would have had no expectation of success in generating antibodies immunospecific for a protein having this sequence.

Thus, the Applicant believes that the Examiner's rejection of the claims based on obviousness over Oka in light of Yoshihara and Goding should properly be withdrawn.

C. The Rejection of Claims Under 35 U.S.C. §112, Second Paragraph, May Properly Be Withdrawn

The Examiner also rejected claim 28 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner cites the phrase in the preamble "said human neuronal ICAM-4 polypeptide," stating it renders the preamble incomplete. The Applicants submit that the cancellation of claims 18 through 32 and addition of new claims 33 through 41 obviates this rejection.

SUMMARY

In view of the amendments and remarks made herein, the Applicants believe that claims 33 through 41 are in condition for allowance and respectfully request notification of the same.

Respectfully submitted,

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Appendix A

33. A method for detecting a human neuronal ICAM-4 polypeptide in a sample, said human neuronal ICAM-4 polypeptide comprising the amino acid sequence set out in SEQ ID NO: 28, said method comprising the steps of

a) contacting the sample with a human neuronal ICAM-4 specific antibody, and

b) detecting an antigen comprising an epitope specifically recognized by an anti-human neuronal ICAM-4 antibody.

34. The method of claim 33 wherein the antibody is a monoclonal antibody.

35. The method according to claim 33 wherein the anti-ICAM-4 monoclonal antibody is selected from the group consisting of the monoclonal antibody secreted by hybridoma 173E, the monoclonal antibody secreted by hybridoma 179I and the monoclonal antibody secreted by hybridoma 179H.

36. The method of any one of claims 33-35 wherein the sample comprises a body fluid.

37. The method of claim 36 wherein the body fluid is selected from the group consisting of serum and cerebrospinal fluid.

38. Hybridoma 179I (American Type Culture Collection Accession No. HB12123)

39. The monoclonal antibody secreted by hybridoma 179I.

40. Hybridoma 179H (American Type Culture Collection Accession No. HB12124)

41. The monoclonal antibody secreted by hybridoma 179H.